the env mRNA. A point mutation (A-C) has converted the *Nla III* site into an *Nco* I site encompassing the env initiation codon where the human ADA coding sequence was inserted (from *Nco* I +74 to Acc I +1324 within the huADA cDNA (▒). Daddona, P.E., et al., J. Biol. Chem. 259:12101-12106, (1984). The Mo LTR/B2 vector was constructed by ligating the 1274 bp *Hind* III-Pvu I fragment of the PEM-ADA vector, Wilson, J.M. et al., Proc. Natl. Acad. Sci. USA 87:439-443, (1990), that contains the B2 mutation (G to A at position +160) to the *Hind* III-Pvu I fragment of MFG. The MPSV enhancer was cloned into MFG by replacing the *Nhe I-Sac* I fragment of the 3' Mo MuLV LTR with the 385 bp corresponding fragment from the 3' MPSV-LTR plasmid (kindly provided by P. Robbins, Pittsburgh, PA) to generate the MPSV-Enh construct. The MPSVE-EnhB2 was analogously derived from MPSV-Enh and PEM-ADA constructs. In the MPSV-LTR construct, the 6014 bp *Ban II-Nhe* I fragment from the pC663neoR plasmid, Ostertag, W., et al., J. gen. Virol. 67:1361-1371, (1986), has been replaced with the 2694 bp *Ban II-Nhe* I fragment from the MFG vector. To generate the Fr-Enh construct, the 450 bp *Nhe I-Kpn* I fragment of MFG was replaced with the corresponding *Nhe I-Kpn* I fragment from the pFr-SV (X) plasmid, Holland, et al., Proc. Natl. Acad.Sci., USA, 84:8662-8666, (1987). Mo-MuLV LTR (□), MPSV sequences (▨), Friend sequences (▒).

(B) α-SGC vector: The α-SGC vector derived from pHSG, bears a portion of *gag* and an enhancer deletion in the 3' LTR, Guild, et al., J. Virol., 62:3795-3801, (1988). In this vector, huADA expression is under the control of the human cytomegalovirus (CMV) enhancer (*Spe*I +154-*Nco* I +515 fragment), Boshart, M. et al., Cell, 41:521-530,

(1985), and α-globin promoter (*Pst 1* -570 -*Nco*I +37 fragment), Braelle, F.E., Cell, 12:1085-1095, (1977).

(C) DNA analysis of NIH 3T3 cells infected with the recombinant retroviruses: After infection of NIH 3T3 cells under standard conditions (see Section 11.1, *infra*), genomic DNA was digested with *Nhe I* and analyzed by Southern blot using a huADA cDNA probe. Each lane was loaded with 10 μg of genomic DNA. The number of proviral copies per cell is indicated under each lane as determined with the Phosphorimager. In the left lane, the copy control corresponding to 1 copy per cell of the Mo-LTR vector.

Figure 12. Analysis of human ADA expression in peripheral blood cells:

(A) Analysis of hADA expression 5-7 months after BMT. The time at which blood samples were drawn is indicated in days after transplantation for each vector. hADA activity was measured by IEF (see Section 11.1., *infra*). The number directly above each sample indicates individual animals. The number of cells injected in every recipient is indicated above and extends from 2 x 10^5 to 4.5 x 10^6 cells. The lower band on the gel represents the activity of the murine endogenous ADA (mADA) and the upper band represents the human ADA (huADA) activity. Control samples were prepared from non-transplanted mice. The italic numbers indicate the mice which were examined in detail in Figure 13.

(B) Fraction of mice expressing huADA at 5-7 months after BMT. Relative ADA activity (r) represents the ratio of the intensity of human to mouse ADA enzyme bands determined on Figure 12A: with the computer densitometer. n_1 indicates the number of